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Winning the Race Against *Frailty*

What are the risks? How can we counteract them?

By Elizabeth Jane Walker

They're draped across shelves, tucked into drawers and strewn across counters. The 142 medals and trophies scattered throughout James Eversull's apartment are the trappings of a committed runner. But to Eversull, those awards have a much deeper significance: They are the result of a pledge he made six years ago.

As a survivor of childhood leukemia, Eversull has always been conscientious about his health. So when he returned to St. Jude Children's Research Hospital in 2008 to participate in a long-term follow-up study, he was confident he would receive a glowing report.

"I'm in good shape; no problem," he told himself.

But the test results told a different story. Problems with his weight, cholesterol, blood pressure and sugar intake put Eversull at high risk for developing heart problems and diabetes.

"That's not going to happen to me," he vowed.

ACCELERATED AGING

Eversull is not the only childhood cancer survivor to identify underlying health problems while participating in a unique study called St. Jude LIFE. Through this program, nearly 3,000 St. Jude survivors have returned to campus to determine how cancer and its treatments affect them as they age.

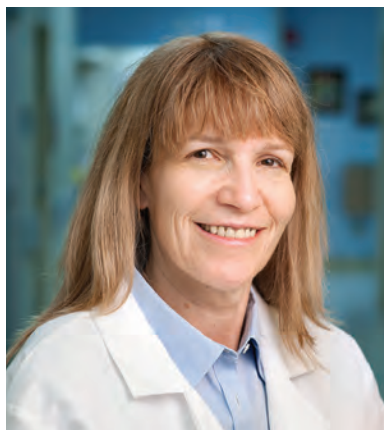
When St. Jude LIFE began in 2007, Kirsten Ness, PhD, of St. Jude Epidemiology and Cancer Control was surprised by the appearance of many of the young adults who were returning for checkups.



As a result of his participation in St. Jude LIFE, childhood cancer survivor James Eversull transformed his life, closely monitoring his diet, working out on a daily basis and completing hundreds of races, including three marathons.

"They would come in for assessments, and I thought, 'These people look like older adults. They walk slowly; they get out of breath; they take a lot of rests; they are weak. They move like people who are elderly,'" Ness says.

She and her colleagues subsequently discovered that childhood cancer survivors are more likely than their peers to experience frail health, including low muscle mass, muscle weakness, low levels of physical activity and fatigue—signs typically associated with aging. In a recent study of 1,922



Kirsten Ness, PhD, of St. Jude Epidemiology and Cancer Control encourages childhood cancer survivors to make lifestyle changes that may help them avoid longterm health issues.

stimulated when survivors stand on a vibrating plate.

Another study involves methods for preventing heart problems. Survivors at high risk for congestive heart failure may enroll in a study testing whether a certain drug can prevent the onset of heart disease.

WINNING THE LONGEVITY RACE

In her daily interactions with survivors, Ness constantly emphasizes the importance of positive lifestyle changes.

“Survivors are given the opportunity—with help from their care providers and their community physicians—to take control of their health by getting appropriate medical screenings, exercising, eating healthy foods, and avoiding tobacco and sun exposure,” she says.

But few people pursue a healthy lifestyle with the vigor and passion of Eversull.

After his first St. Jude LIFE evaluation, Eversull began working out in the gym five days a week, running seven miles each day and closely monitoring his sugar intake. The hundreds of road races he has completed include three marathons. After outrunning acute lymphoblastic leukemia, Eversull is now determined to win the longevity race.

“There’s a man in my town who is still running races at age 95,” Eversull says. “I told my doctor that if I can keep up what I’ve been doing and maintain my healthy lifestyle, I don’t see why I can’t live to be 120.” ■

survivors with an average age of about 34, the researchers identified more than 13 percent of women and 3 percent of men as being frail. In a comparison group from the general population, no individuals qualified as frail.

“The survivors’ overall physical well-being essentially resembles that of people 30 years older than they are,” Ness says.

COUNTERACTING THE PROBLEMS

The hospital’s scientists are devising ways to counteract the problems experienced by these survivors.

“In our brain tumor population at St. Jude, we’re testing the effects of doing high-intensity exercise during radiation therapy,” Ness explains. “So while they’re undergoing cancer therapy, they’re exercising.”

In an effort to increase bone health in survivors with osteoporosis, scientists are testing whether bone health is

Brandy Wilbanks (at left) participates in a test as part of the St. Jude LIFE study. Results showed that this young mother had the fitness level of a woman in her mid-60s. “Most 32-year-olds don’t have to worry about breaking a hip, but I have to,” says Wilbanks, who had bone cancer in her leg when she was a teen. Wilbanks is making a concerted effort to improve her health by exercising, eating the right foods and avoiding unhealthy habits such as excessive sun exposure and smoking. She also has regular medical checkups and tests, based on recommendations from her St. Jude physicians.



The Heartbeat of the Hospital

By Elizabeth Jane Walker

Why is care exceptional at St. Jude? Our nurses offer 9 compelling reasons.

They are clinicians. Researchers. Listeners. Advisers. Cheerleaders. They calm patients in their first terrifying moments and walk alongside them for the rest of their treatment journeys. Every patient knows that nurses are the heart and soul of St. Jude Children's Research Hospital.

The 670 nurses who practice at St. Jude offer a unique perspective on the care offered to children and families. Why do these individuals choose to expend their energies at St. Jude instead of somewhere else? Our nurses offer nine simple reasons.



ANN-MARGARET HEDGES

1 We have freedom to focus.

Surgery is scary; having cancer is scary. In the Recovery Room, I have one patient, and I can focus on that child. I can do everything I need to do with that child, and then I feel like, "Wow, I did a great job!" Families are comforted to know that I'm focusing all of my attention on their child.

One mom once told me, "You know, I used to be anxious about my child during surgery. But when I know that you're in there, I know she is going to be taken care of."

*Patricia Davis, BSN, RN, CPAN
Operating Room, Recovery*

Patricia Davis and Jesse James



John Franklin and Jaxon Johnson

We help families cope.

In a regular hospital, a kid might come in for something like appendicitis, which stresses the family for a short time. But our families have that high stress level for months or years at a time. A couple of days' stay in the hospital might be no big deal—but when you start doing this long-term, you're dealing with acceptance. Yesterday, the parents had a perfectly healthy child, and today they have one who has cancer.

We help parents realize that they have to take care of themselves so they can take good care of their child. We help them through this experience, and in the process we sometimes get to see miracles happen. People ask me how I can keep working in pediatric oncology, and I tell them that it's because of the impact we make on the lives of these families.

*John Franklin, BSN, RN
Inpatient, Solid Tumor*

Our voice is heard.

After working elsewhere, I can tell you that St. Jude is a great place to work if you're a nurse. I often tell people that my worst day here doesn't even compare to my best day somewhere else. At St. Jude, the doctors and nurse practitioners seek out my opinion. I'm on committees where I have a chance to help make important decisions. That's really refreshing.

Here, I'm part of a team, and they have confidence in my assessment as a nurse. We all work together for the patient.

*Nicole Thomas, RN, APHON
Medicine Room*



Nicole Thomas and Jesse Hall

4 We are always learning.

When I came to St. Jude 13 years ago, I had an associate's degree in nursing. Now, I have a bachelor's degree, a master's degree and two additional certifications. St. Jude supports us as we further our education, and they listen to our ideas.

People ask me all the time, "Now that you have your master's degree, what are you going to do?" I tell them, "I'm going to continue doing what I've been doing—taking care of my patients." At St. Jude, nurses are respected by physicians and our other colleagues. That means a lot, because we have valuable ideas and experience and opinions to offer.

LeeNedra Jackson, MSN, RN, CNL, CPN
Surgical Services, Sedation

SETH DIXON



LeeNedra Jackson and Coraliz Martinez

5 We care for the entire family.

We are there from Day One, when a child arrives as a brand-new patient, all the way through their care. I'm that child's nurse, no matter where they go in the hospital. Staff members in other areas will call me if they have questions or issues about that child. As a result, patients and parents don't have to go through their story every time they come to the clinic. As part of that process, you learn things about them—I know that one child needs his pacifier when he gets IV sticks and that he needs a certain teddy bear.

I might get a phone call from a family in Louisiana who needs refills of home medicines mailed to them; I might get a call from a parent who has had a flat tire on the way to the hospital and needs transportation; I might help a sick mom find local medical care while she's in Memphis. My job is to take care of the children and their families, and I do the best that I can.

Julie Morganelli, BSN, RN, CPHON
Ambulatory Care Unit, Solid Tumor



ANN-MARGARET HEDGES

Bailee Christianson and Julie Morganelli

6 We embrace the magic of childhood.

On the transplant unit, the families stay from a couple of weeks to months—and I really get to build relationships with them. One patient I particularly liked to take care of is also the sassiest 5-year-old I have ever met. She has big, brown eyes and a mischievous smile. Every day with her morning medications, she would take a pill that was in a blue capsule. This pill was special; it was her “Cinderella” pill. After she took it, she transformed into “Cinderella, the boss princess.”

Every day “Cinderella” would dress up and walk the hallways. One particular day after putting on her fairy wings and crown, she told me to kneel down and close my eyes because she had a surprise for me. She placed a plastic crown on my head and told me that I was now also a princess. We would walk along the hallways until we found a corner to hide behind. When an unsuspecting nurse would walk by, we would jump out and roar!

Maggie Ho, BSN, RN, CPN

Bone Marrow Transplantation and Cellular Therapy

ANN-MARGARET HEDGES



Aaron Rucker and Tammy Teems

7 We practice health care like it should be done.

My parents were hospitalized at two different facilities. As a patient, as a family member and as a nurse at another institution, I heard people talk about treating the patient and family. St. Jude truly does that, and it makes a huge difference. I recognized that the first time I ever set foot here. I walked into the lobby and listened to a group of teens talking about their experiences. The atmosphere seemed more family centered than anything I'd seen before. You have kids walking around in their PJs and doing their daily routine. This is their world, and they are doing their thing.

When I go home at the end of each day, I know I have done what I'm supposed to be doing. This is how health care is supposed to work. I think the adult community and the community outside of St. Jude could learn a lot from us.

Tammy Teems, RN
Assessment-Triage

SETH DIXON



Montero Thurston-Smith and Maggie Ho



Michelle Mosby (at right)

We devote our lives to the mission.

Working in the ICU is stimulating, both mentally and spiritually. During the past 35 years of working at St. Jude, I've had the opportunity to see the long-term results of the hospital's research—I've seen where we were and where we are now. The work is difficult, but we also get to see the results of the care that we give individual patients.

It's exciting when former patients come back to see us. They may not remember us—many times their condition was so critical that they don't remember anything about that time—but their parents sure do. We can see how we play a part in people's lives and the impact that our work has.

*Michelle Mosby, RN
retired February 2014 from Intensive Care Unit*

We are partners in the journey.

When families arrive at St. Jude, they're often shell-shocked. They may have been told, "Your child has an incurable disease. We don't know how to treat it, but St. Jude does."

At first, they think the end of treatment will never come. We love seeing them perhaps 120 weeks later at the last off-therapy visit, when they say, "Well, we never thought we would see this day, but now we almost don't want to leave St. Jude." It's a good feeling when they say that.

*Tony Tiscia, BSN, RN, BA
Procedures*



Tony Tiscia

St. Jude Nursing by the Numbers

- More than **670** nurses work in **32** departments.
- About **450** of those nurses work in direct patient care.
- Overall nurse-to-patient ratio: **1:3**
- ICU nurse-to-patient ratio: **1:1**
- Nurse with the longest tenure has worked at St. Jude **41** years
- Number of weeks new nurses attend orientation: **12**
- Percentage of RNs with baccalaureate or higher degree: **72%**
(national average is 55%)



St. Jude surgeons are world renowned for innovative approaches that save the lives of children with cancer and other diseases.

When Precision Counts

By Joyce M. Harris

Mick'el Wilson was 15 months old when his grandmother noticed that he had blood in his diaper and a firm, bloated belly. After examining the toddler, doctors discovered that Mick'el had advanced bilateral Wilms tumor, a cancer of both kidneys.

"I was shocked. Scared," says Mick'el's father, Tommie.

When chemotherapy and radiation failed to shrink the tumors, doctors at their local hospital announced there was nothing more they could do.

"I didn't want to sit on the front row at a funeral," recalls Mick'el's mom, Tameka.

The family requested a second opinion, and within days Mick'el was under the skilled care of Andrew Davidoff, MD, Surgery chair at St. Jude Children's Research Hospital. The renowned surgeon is an expert in bilateral Wilms tumor.

Davidoff and his colleagues perform about 1,600

operations each year to diagnose and treat cancer and other life-threatening diseases. They partner with St. Jude oncologists, radiation therapists, pathologists, anesthesiologists, nurses and basic scientists to plan and deliver the best treatment for children with solid tumors. Their specific expertise includes complex surgical procedures to treat kidney, neuroendocrine, eye and bone cancers.

"In addition to the technical aspects of these procedures, understanding what is appropriate for each patient is even more important in children with cancer," Davidoff says. "It means knowing when surgery is appropriate and when it is not. If surgery is appropriate, is the best timing before or after chemotherapy? How aggressive or conservative should we be with the surgery, and is surgery the only way to cure the cancer?"

Built for children

St. Jude will soon have a new operating room and surgery complex that will double the size of the current space. The new facility is designed to provide optimal care to patients and families who look to St. Jude for treatment and to further the hospital's commitment to education and training. The facility will include:

Integrated Operating Rooms with imaging and pathology services to encourage real-time interaction during surgery

Adjacent Intensive Care Unit (ICU) to reduce transport time for critical patients for surgery

Spacious, connecting parent rooms in the ICU

High-tech observation rooms to train surgeons and fellows from around the globe, which will help improve outcomes for children worldwide.

Nearly every new pediatric surgeon in the U.S. and Canada participates in training at St. Jude.

Air-filtration technology to maintain a germ-free environment

State-of-the art technology to better assess how cancer affects the eye in children with retinoblastoma and other diseases that secondarily affect the eye

A modular design to incorporate the latest surgical equipment as technology advances

Preserving kidney function

Bilateral Wilms tumor occurs in only 30 U.S. children each year. Nearly 20 percent of those children have their surgery performed at St. Jude.

"Because of our extensive experience surgically managing children with cancer, I feel we have a more aggressive willingness to perform complex surgical procedures rather than saying they can't be done," Davidoff says. "While most other surgeons would remove one or even both kidneys, our approach is to save as much normal kidney on both sides when possible. That's where experience counts."

Not only does this approach, called nephron-sparing surgery, maintain excellent survival rates, but it also helps children with this rare cancer avoid kidney failure, dialysis and transplantation. The No. 1 goal is always cure, but improving quality of life is a priority as well.

Davidoff surgically removed a softball-sized mass from Mick'el's left kidney and another the size of a tennis ball from his right kidney. Today, the active 9-year-old is five years cancer-free with normal kidney function.

Davidoff has performed more than 50 such surgeries and publishes the results so the medical community can learn from the St. Jude model. Early results from cases like Mick'el's show promise not only for cures but for avoiding complications after surgery.

Experience and expertise

Neuroblastoma is the most common solid tumor in children next to brain tumors and accounts for 7 to 10 percent of all childhood cancers in the U.S. By the time neuroblastoma is diagnosed, the cancer has usually spread to other parts of the body. Outcomes for the disease vary widely.



A cuddly teddy bear patiently awaits the return of its owner, who is undergoing an operation in the St. Jude surgical suite.

“In some children, the disease can be very non-aggressive,” Davidoff says. “We remove the tumor with surgery, and the children are cured. Others with advanced disease may require surgery, chemotherapy, radiation and bone marrow transplantation and still the survival rate is only 30 percent.”

When venturing into this complex territory, St. Jude surgeons meticulously separate the tumor from delicate blood vessels that nourish the kidneys, liver, intestines and other structures. The surgery requires precision and skilled hands to prevent damage to vital organs.

“It’s a challenging and tedious surgery in which we have a lot of experience and expertise,” Davidoff says.

St. Jude surgeons also team with oncologists to incorporate new surgical techniques and approaches into clinical trials for neuroblastoma.



PHOTOS BY ANN-MARGARET HEDGES

“Because of our extensive experience surgically managing children with cancer, I feel we have a more aggressive willingness to perform complex surgical procedures rather than saying they can’t be done,” says Andrew Davidoff, MD, St. Jude Surgery chair.



When doctors at another hospital ran out of options to treat Mick'el Wilson's aggressive kidney tumor, his mom obtained a referral to St. Jude. "I didn't want to sit on the front row at a funeral," she says. Andrew Davidoff, MD, surgically removed a softball-sized mass from Mick'el's left kidney and another the size of a tennis ball from his right kidney. Today, Mick'el is a bright and energetic 9-year-old with normal kidney function.

Improving care for children with eye cancer

The St. Jude retinoblastoma treatment team is one of the most recognized in the country and is a textbook example of how research in St. Jude laboratories improves outcomes for patients in the clinic.

"Our basic scientists are able to develop preclinical models and identify pathways we can exploit with novel targeted therapies that we hope will reduce the toxicity of treatment, preserve vision and make patients' lives better," says Matthew Wilson, MD, ocular oncologist. He and Rachel Brennan, MD, a pediatric oncologist and retinoblastoma expert, are part of the team that treats children with retinoblastoma.

"The ability to examine and observe the eye and understand the size and number of tumors in the eye is just as important as treatment," Wilson says. "With aggressive surveillance and careful examination of the eye, we're able to judiciously apply the laser and cryotherapy to treat tumors, save the eye and preserve as much vision as possible."

In addition to the retinoblastoma group, patients receive support from an eye clinic and many other services both during and after therapy. Because of this teamwork, the hospital's investigators recently achieved a 100 percent five-year survival rate for children with retinoblastoma in one or both eyes at diagnosis.

Researchers continue to create new treatment options for patients whose cancer has spread beyond the eye, as well as develop new routes for delivering drugs while avoiding radiation and minimizing long-term effects of therapy.

Saving lives and limbs

When Bhaskar Rao, MD, joined St. Jude in the 1980s, amputation was inevitable for children facing surgery for osteosarcoma and Ewing sarcoma, the most common bone cancers in children. St. Jude was one of the few centers that offered an alternative—saving their limbs as well as their lives.

Today, the offer still stands as St. Jude surgeons help children maintain function of their arms and legs.

"Approximately 90 to 95 percent of our patients with bone tumors will have some sort of limb salvage," says Rao, a pioneer in limb-sparing procedures. "Our approach is chemotherapy to shrink the tumor to an operable size; then we perform the limb-sparing surgery."

Rao and orthopedist Michael Neel, MD, remove the diseased bone and replace it with a custom-made, expandable prosthesis. Because bone cancer primarily affects adolescents, growing patients return to St. Jude for outpatient procedures to lengthen the prosthesis and to maintain the same limb length on either side. After surgery, children



The surgery team at St. Jude performs about 1,600 operations each year to diagnose and treat cancer and other life-threatening diseases.

undergo extensive rehabilitation and support care to help them maintain normal function.

The local recurrence rate for St. Jude patients who have undergone surgery for Ewing sarcoma is below the 10 percent national average. Rao attributes the outcome to experience, supportive care and unmatched follow-up care.

“At some centers, the surgeon operates on patients and sends them back to the oncologist and then the surgeon

never sees the patient again until they encounter complications,” Rao says. “Here, we provide continuity of care for patients until they are 18 years old or until 10 years after diagnosis, whichever comes later.”

Patients treated at St. Jude are eligible to receive comprehensive screenings and health assessments related to their cancer—for a lifetime.

“This level of follow-up care is not available in many places,” adds Rao, who also serves as Surgery director for the St. Jude International Outreach Program.

Looking ahead, surgeons are evaluating and exploring new limb-sparing techniques to improve survival and help children live normal lives after treatment.

Minimally invasive techniques

Minimally invasive surgery is an alternative approach to diagnose and treat solid tumors, depending on the size and location of the tumors. John Sandoval, MD, uses the tools of the trade to view and investigate tumors in the chest and abdomen. He makes small incisions to perform biopsies, sample lymph nodes and remove abdominal tumors and lung lesions.

“We are staying mainstream and contemporary and attempting to push the envelope in laparoscopic surgery in children with solid tumors,” Sandoval says.

There are advantages for patients who qualify for the technique: less pain, quicker recovery, a speedy return to therapy and fewer long-term functional complications.

In 93 percent of procedures performed between 1994 and 2004, patients were able to receive an accurate diagnosis relying solely on the minimally invasive techniques performed at St. Jude. A follow-up study will be published this year to identify improvements and trends from the past decade. Sandoval anticipates the success rate to rise to nearly 100 percent.

Minimally invasive surgery is relatively new to pediatric oncology when compared to traditional surgery. Sandoval and his colleagues are helping to establish consensus guidelines for the appropriate use of these techniques in children with cancer. This provides the ideal opportunity for St. Jude to help shape the future of minimally invasive surgery in pediatric oncology. ■

Building on **Our Strengths**

Promise talks with Dr. William E. Evans, St. Jude director and CEO, about the hospital's achievements and future direction.

You've worked at St. Jude for many years, beginning as a student. **WHAT have been some of the most significant changes?**

It's easy to say how much the campus and the organization have grown in size, but I think the most impressive aspects have been the quality of people we've been able to recruit and retain, the quality of the programs we've built, and the importance St. Jude has assumed on a global scale. In spite of our physical growth, we've worked hard to retain the feel of a relatively small place and our culture of compassion, collaboration, innovation and quality. People know each other; they work together: they interact and innovate. It was a major achievement that this did not change while we were growing. Sustaining these interactions and collaborations is why our productivity and creativity remain exceptional.

****WHAT** sets St. Jude apart from other research institutions?**

There are few places in the world where basic science and patient care are as well integrated as they are at St. Jude. We have incredible people and incredible support from the public, which give us the resources we need to be like no other place—to try things that other places can't try. We place great importance on doctors and scientists knowing each other and working together. It's an intrinsic part of our culture, and we design our facilities and infrastructure to facilitate this. For a scientist who's working at that interface of patient care and research, there isn't a better place to do that kind of work than here.

At most other academic medical centers, the biochemists, pharmacologists and geneticists are on one side of campus, and the hospital and doctors are on the other side of campus. Often, those groups rarely meet or

intersect. Whereas at St. Jude, week in and week out, we focus on how we can integrate the scientists, doctors, patients and staff. This is one thing that attracted me to St. Jude in 1976 and a major reason, beyond our mission, that has kept me here for my entire career.

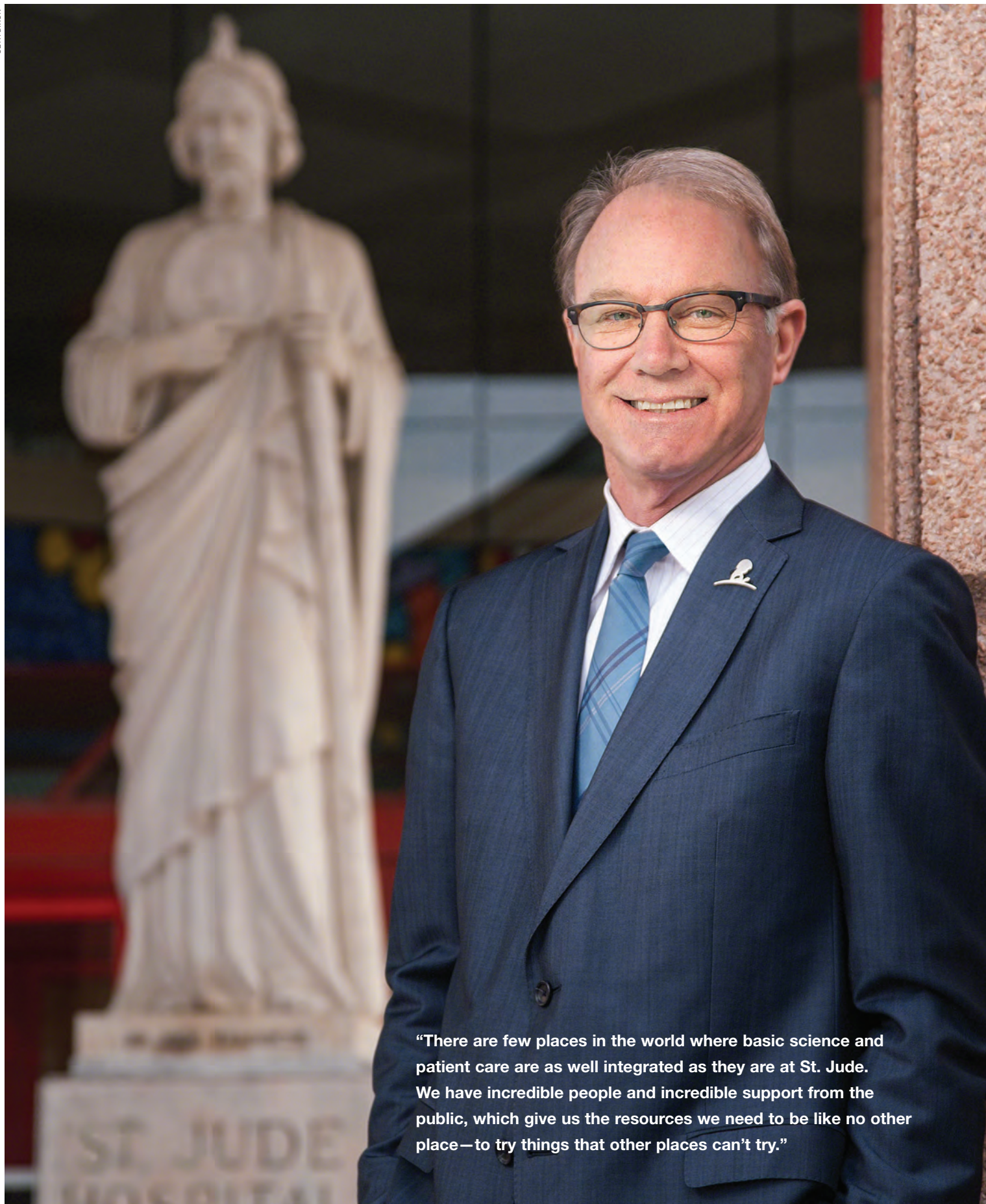
****HOW** does St. Jude foster that integration?**

Dr. Don Pinkel, the first director at St. Jude, basically said, "We're going to organize everything around the patient—so the science needs to connect to the patients, and the patients and doctors need to connect to the scientists." In the last 20 years, the entire scientific community has moved toward that model, which is called translational research. St. Jude was doing this before these buzzwords were created.

We've continued to do things to make the interaction between doctors and scientists a natural one and to keep that small-institution feel. We often place laboratory research in the same building as patient care or clinics. In our newest building, for example, the proton therapy center, Surgery and the ICU are going to be in the same building as research labs. In that way, many of our buildings are a microcosm of the greater campus, which focuses on people working in collaboration. This also enriches the environment for those doing pure basic science that may be many steps removed from translation, because every day they see the ultimate benefactors of their fundamental discoveries, our patients.

****HOW** will St. Jude remain on the cutting edge of research going forward?**

It has been interesting to see how much technology has evolved in the last decade—how that technology has accelerated science, changed the scale of research we can do, and accelerated the pace at which we can understand what causes childhood cancer and how better to treat it. It's hard to



“There are few places in the world where basic science and patient care are as well integrated as they are at St. Jude. We have incredible people and incredible support from the public, which give us the resources we need to be like no other place—to try things that other places can’t try.”



SETH DIXON

Cracking the G-gnome

"There's a little ceramic gnome on my desk, with a crack on his hat, which is emblazoned with the letter 'G,'" Evans says. "Brennan Simkins and his father, Turner, came into my office one day and gave it to me. They said, 'Thanks for all the work you're doing to crack the G-gnome.' To me, that clever little memento is a reminder that our patients and families know about what we're doing in the laboratories. They know how important it is to integrate the treatment with the science, and they understand the importance of our Pediatric Cancer Genome Project. It is patients and parents like these who constantly remind us of the importance of the work we're doing and their partnership in this grand endeavor."

Some of it is going to be immunotherapy and other biological therapies. It will be improved surgery; more targeted radiation therapy, such as proton therapy; and better supportive care.

We will continue to use genetics as a diagnostic to personalize therapy based on the DNA in the cancer cells and also the normal DNA that children inherit from their parents. These differences affect how

imagine what things are going to be like in 10 years, because it's moving so quickly. An organization has to move quickly while staying focused and remaining committed to quality. For St. Jude, it's not just how fast we do it; it's how well we do it. It's not how big we are; it's how much better we are at doing things. By keeping that attitude first and foremost, St. Jude will continue to be the best at what it does.

WHAT is the future of genetics research?

Genetics research will continue to accelerate; sequencing DNA and other interrogations of DNA will become faster, less expensive and more robust. It is going to become increasingly automated. The real challenge is going to be interpreting the onslaught of data. We're now generating data in days what used to take years to generate. The greatest power comes from integrating all of the different genomic technologies with our patient outcomes to understand what is driving childhood cancers and what is influencing treatment response. Our challenge is to translate the power of genomics into better treatment, and we are doing that. We are also harnessing these technologies in our gene therapy program, making remarkable advances against several genetic diseases, like hemophilia and immunodeficiencies.

WHAT will it take to meet our goal of pushing childhood cancer survival rates to 90 percent in the next decade?

It is going to take new medications as well as new treatment strategies. But it's not all going to be medications.

children respond to drugs and other treatments.

Discovering what happens in the genome to make a normal cell become a cancer cell is the path to finding better treatments and pushing overall cure rates for childhood cancers beyond 90 percent. It's going to be a challenge, but we are already there in leukemia. There are still some cancers—some forms of brain tumors, some solid tumors—where overall cure rates are still around 50 percent. We need major advances and discoveries that will lead to new treatments, new drugs and new approaches. It's going to happen, and St. Jude is going to lead the way.

WHAT gives you the most inspiration for your work here?

I think the most inspiration comes from the patients and their treatments getting better—not only improvements in cure rates, but reducing the burdens of treatment. That's why the work that goes on here is so important: We're trying to tip the scale in favor of better success and less toxicity in treatment, to not only improve cure rates but enhance quality of life for childhood cancer survivors. That's why treatment of all childhood cancers—even acute lymphoblastic leukemia, with its 90 percent cure rate—must be further improved.

The more we know about what causes these cancers and what determines response to treatment, the better chance we have of improving both cure rates and quality of life for children with cancer.

10 Years of Progress

“An organization that moves as quickly as St. Jude—that is as entrepreneurial as we are—must redefine itself every seven to 10 years to ensure it continues to define the forefront of science and medicine,” observes Dr. William E. Evans, St. Jude director and CEO. “As a result, we are continuously launching new programs and new initiatives.”

Here, Evans lists a few of the significant accomplishments that have occurred during the past decade:

- **Comprehensive Cancer Center designation.** In 2008, the National Cancer Institute (NCI) designated St. Jude as the nation's only Comprehensive Cancer Center devoted solely to children. In its last report, the NCI gave us a ranking of “exceptional,” which is the highest ranking possible.
- **Advancement of personalized medicine.** We have built decision support into our electronic medical record so we can routinely use genetic information to tailor treatment. We also founded and are leading the international consortium that is establishing guidelines for how to use pharmacogenomics in patient care.
- **Creation of the St. Jude LIFE study.** This program is telling us things about children we cured 10, 20 and 30 years ago. Former patients are returning to campus as adults for us to assess their health in the clinic and advise them on maintaining their health going forward.
- **Launch of the Pediatric Cancer Genome Project.** This unprecedented project is the largest investment to date aimed at understanding the genetic origins of childhood cancers. The St. Jude – Washington University Pediatric Cancer Genome Project has proven to be very powerful and crucial to our drug-discovery programs and our future. We are also freely sharing data generated from this project; that data has been downloaded by investigators around the world.
- **Creation of a new department of Chemical Biology and Therapeutics.** This department focuses on drug discovery and brings robotics and technology onto this campus to capitalize on the discoveries emerging from the Pediatric Cancer Genome Project and individual investigators at St. Jude.
- **Construction of a proton therapy center.** This facility will be second-to-none in terms of technology. It will also be the only proton beam in the world focused solely on children and how to treat childhood cancers with proton therapy. The importance of having this on campus is that we can integrate it with all of our other treatment and research.
- **FORTUNE 100 Best Companies to Work For.** The key to our success is recruiting great people and giving them what they need to do their best work. *FORTUNE* magazine has for the last four years listed St. Jude as one of the top places to work. That gets the word out about what St. Jude is doing and why it is a great place to work.
- **The Global Education Collaboration Center.** When this center opens on the St. Jude campus later this year, it's going to be a great space for interaction and teaching—where we can host major national and international conferences to tell people about what's going on at St. Jude. It will become an intellectual hub of our campus.
- **The perfect score we received from The Joint Commission.** The Joint Commission had no recommendations for improvement. This almost never happens, anywhere. It is a testament to the quality of our patient care, our people and our facilities.
- **Danny Thomas Place.** By changing our mailing address to 262 Danny Thomas Place, we celebrate and recognize our founder every day in our correspondence. The number 262 represents our founding date in February of 1962. This may seem trivial, but staying connected to your roots and telling the world about the vision of Danny Thomas are really important.
- **Celebration of our legacy.** By erecting a statue to Danny Thomas on campus and building a Wall of Honor for our most distinguished deceased board members, we celebrate our legacy of leadership as we welcome people to our campus.

What Is a CLINICAL TRIAL?

Families and researchers join forces to improve survival rates, reduce side effects.



ANN-MARGARET HEDGES

St. Jude has created more clinical trials for cancer than any other children's hospital. Alexis Jenkins (center) has participated in several clinical trials for neuroblastoma. She and her mom, Bridgette (at right) consult with Nurse Practitioner Katie Birdsell during a recent clinic visit.

By Joyce M. Harris

Alexis Jenkins has had her share of peaks and valleys during her battle with stage 4 neuroblastoma. In the 5½ years since her local pediatrician referred her to St. Jude Children's Research Hospital, her cancer has returned three times. Yet, through it all, her parents find solace in knowing their easy-going yet resilient 8-year-old has options.

The family's journey to St. Jude began when Alexis was a toddler having persistent night fevers. Doctors referred Alexis to the hospital after testing revealed low blood counts and masses in her chest. When Roger and Bridgette Jenkins arrived at St. Jude, they learned about the tumors in Alexis' abdomen, bone marrow, chest and along the tissue near her spine.

Because the cancer had spread to other parts of Alexis' body, there was a strong chance standard treatment would not result in a cure. Clearly, Alexis needed something different.

From lab to clinic

St. Jude has created more clinical trials for cancer than any other children's hospital. Many of these are studies that originate

from discoveries made in the hospital's labs.

In a clinical trial, investigators ask important research questions and provide a plan with detailed instructions on how they aim to answer the questions and the results they hope to achieve.

"The collaboration between laboratory scientists and clinical researchers is well integrated at St. Jude. It's a continuous loop of information where the laboratory feeds ideas for the next generation of clinical trials, and what we learn in the clinic is used to feed the science in the laboratory," says Victor Santana, MD, vice president for Clinical Trials Administration at St. Jude.

When Alexis' cancer returned after standard therapy, Roger and Bridgette enrolled their daughter in several clinical trials.

"Before we enrolled Alexis in a clinical trial, we asked lots of questions," Bridgette says. "We wanted to know what they had learned from the laboratories. Will the benefits outweigh the side effects? We wanted to learn as much as we could so we could determine if it was the right option for our child."

More treatment options

In early-phase studies involving new agents or existing drugs, the goal is to determine a safe dose of the new agent in a small group of participants. Once a safe dose is established, researchers test to see how well the cancer responds.

Alexis participated in early-phase studies with some good responses, but her cancer inevitably returned. In 2010, her parents enrolled Alexis in another clinical trial using a new antibody therapy to attack her cancer. She responded well, and her disease went into its longest remission. This antibody has now become an integral part of St. Jude neuroblastoma therapy.

“At St. Jude, patients can participate in a multitude of clinical trials. That’s important, because it gives the children access to the latest therapy that could potentially benefit them,” Santana says. “Because they have participated in trials before and we know their history, their participation becomes a rich source of information in terms of understanding how they may respond to future treatment.”

Creating new standards of care

Doctors have used what they learned from Alexis and others in the study to develop a similar clinical trial for patients with newly diagnosed neuroblastoma. If children in that study continue to respond well, researchers will test to see how well the experimental drug compares to standard therapy or whether that drug can be combined with standard therapy.

If the response rate is better than the current treatment, then the experimental therapy will become the new standard of care. Safety and review committees at St. Jude carefully monitor each clinical trial throughout each phase to balance the science and the safety of research participants.

“We want to make sure the science is incorporated into clinical trials in a way that we maximize the potential for benefit and minimize the risk for those who volunteer to participate in clinical research,” Santana says.

PETER BARTA



At St. Jude, “the laboratory feeds ideas for the next generation of clinical trials, and what we learn in the clinic is used to feed the science in the laboratory,” says Victor Santana, MD, vice president for Clinical Trials Administration.

Partners in care

Research grants and gifts from St. Jude supporters enable investigators to leave no stone unturned when it comes to seeking new treatment options, with fewer side effects, for Alexis and other children with tough-to-treat cancers. Those funds give St. Jude investigators the freedom to focus on what’s best for each child.

Equally important are the partnerships St. Jude has established with other institutions.

“Pediatric cancer is rare. This poses a challenge, because some trials do not have enough patients to open or the trials close early because not enough patients are enrolled,” Santana says. “As pediatric oncologists, we have to join forces with others throughout the nation and the world to develop methodical

clinical trials. That helps us get the best answers to our research questions and identify the best treatment options for our patients.”

Looking ahead

“If it weren’t for our decision to enroll Alexis in clinical trials, she would not be with us today,” Roger says.

Alexis received stem cells from her mom as well as from her sister, Hanah, for bone marrow transplantations. Thus far, all of the healthy stem cells donated by Hanah have engrafted into Alexis’ bone marrow.

Doctors will continue to follow Alexis’ progress. Her parents hope that her cancer stays in remission as they rely on their faith and support from family, friends and clinicians at St. Jude to get them through the days ahead.

“It’s comforting to know that St. Jude has so many options for our child,” Bridgette says. “I’m sure the doctors learned a lot from us because we were willing to participate in clinical trials. Somebody has to be willing to try it. If one kid tries it and it works, then that person can make it better for the next child. All of us have to work together so we can continue to have advances in medicine.” ■

Learn more: stjude.org/clinicaltrials

Research Highlights



SETH DIXON

New clues for fighting ALZHEIMER'S DISEASE

St. Jude scientists have made a surprising connection between a rare disorder that strikes young people and Alzheimer's disease, a disease that usually affects older adults. The connection is an enzyme that nerve cells use to recycle or dispose of unneeded proteins. Young people with the disorder sialidosis have too little enzyme. A recent study suggests the enzyme might also play a role in Alzheimer's disease.

Individuals with Alzheimer's disease develop plaques in their brains made of abnormal clumps of protein. In laboratory studies, St. Jude researchers found that increasing enzyme activity may reduce the number of plaques in the brain. The research was led by Alessandra d'Azzo, PhD, of St. Jude Genetics (center), who is pictured with colleagues Ida Annunziata, PhD (at left), and Annette Patterson (at right). The research appeared in the scientific journal *Nature Communications*.

"This is the first time this enzyme has been linked to Alzheimer's disease. We hope it will lead to better tools to diagnose as well as slow, or even reverse, the disease in some patients," d'Azzo said.

BRAIN TUMOR culprit caught

Scientists at St. Jude recently led a successful hunt through billions of pieces of genetic information. Their prize? The discovery of an abnormal protein that likely spurs cancer growth in children with the brain tumor ependymoma.

The abnormal protein turns normal cells into cancer cells by stimulating a process called NF- κ B signaling at the wrong time. The problem was found in 70 percent of children with ependymomas in the front part of the brain.

There are no effective drugs against ependymoma, so scientists are actively seeking new therapies. "This should help us to understand how abnormal NF- κ B activity drives cancer. Then we can develop new treatments to block that activity," said Richard Gilbertson, MD, PhD, director of the St. Jude Comprehensive Cancer Center.

The findings, published in the journal *Nature*, are the latest from the St. Jude Children's Research Hospital—Washington University Pediatric Cancer Genome Project.

OLD FLU VIRUS still threatens

St. Jude scientists warn the flu virus that caused a pandemic in the 1950s remains a threat today. The risk is greatest for those under age 50; this group lacks immunity to the virus.

The warning follows results from a new study—the most complete analysis yet of H2N2 influenza A strains found in poultry and wild water birds. "This research suggests that H2N2 could re-emerge as a significant threat," said Robert Webster, PhD, of St. Jude Infectious Diseases.

The good news from the study is that current antiviral drugs may be effective against this flu strain. An existing vaccine may also provide protection. The study appeared in an online edition of the *Journal of Virology*.

Taking aim at a GLOBAL KILLER of kids

Antibiotic resistance is a growing global concern, especially in bacteria that cause serious diseases, such as tuberculosis (TB). This disease kills 1.3 million people a year, and extremely drug-resistant TB has been reported in dozens of countries.

St. Jude scientists recently led a project to re-engineer an existing weak antibiotic into a TB killer. Chemical changes to the original drug prevent TB bacteria from flushing the new antibiotic out of their system.

The new antibiotics work well against drug-resistant TB, and appear to be safe and effective in laboratory studies.

“We are now working towards the next key step: testing these antibiotics in a clinical trial of patients with drug-resistant TB,” said Richard Lee, PhD, of St. Jude Chemical Biology and Therapeutics.

The findings were reported in *Nature Medicine*.

Good FORTUNE

For the fourth consecutive year, St. Jude has made *FORTUNE* magazine’s list of the “100 Best Companies to Work For.”

The list recognizes companies with exceptional workplace cultures that foster high employee morale and dedication. Companies are graded based on employee surveys and questionnaires about company programs and practices. St. Jude employees give particularly high ratings to their pride in working

for the hospital and their ability to make a difference.

“This recognition not only serves to inspire all of us who work here every day; it also helps us recruit and retain the very best people,” said Dr. William E. Evans, St. Jude director and CEO.

More than 252,000 employees at 257 companies participated in the most recent survey.

Stressing CANCER out

Even cancer cells can feel stress. In fact, it can kill them. According to new research led by St. Jude, drugs that enhance a process called oxidative stress may offer a new way to combat an aggressive soft tissue tumor called rhabdomyosarcoma.

Clues hidden deep within the DNA of tumor genomes suggested that rhabdomyosarcoma cells may experience high levels of oxidative stress. To exploit this potential weakness, the researchers used drugs to boost the levels of oxidative stress still higher. The tumor cells died.

“This suggests that altering the ability of tumor cells to

handle that stress—or increasing the stress just a bit—is enough to push the cell over the edge, and it dies,” said Michael Dyer, PhD, of St. Jude Developmental Neurobiology, who is a Howard Hughes Medical Institute Investigator. “This gives us novel and exciting new therapeutic options to pursue.”

The research also revealed that two key types of childhood rhabdomyosarcoma have different underlying genetic causes and provided insights into why tumors sometimes come back after treatment. The findings, published in *Cancer Cell*, are the latest emerging from the St. Jude Children’s Research Hospital—Washington University Pediatric Cancer Genome Project.

Highlights



Sherr inducted into American Academy of Arts and Sciences

Charles Sherr, MD, PhD, St. Jude Tumor Cell Biology chair, and Howard Hughes Medical Institute Investigator, signs the American Academy of Arts and Sciences' Book of Members during an induction ceremony in Cambridge, Massachusetts. Sherr was among 164 of the nation's most influential artists, scientists, scholars, authors and institutional leaders who were inducted into the American Academy of Arts and Sciences. Founded in 1780 by John Adams, the academy is one of the nation's oldest and most prestigious learned societies, and an independent research center that draws from its members' expertise to conduct studies in science and technology policy, global security, the humanities and culture, social policy, and education.

Waking up the BODY'S DEFENSE system

Blood contains a large number of T cells, which act like soldiers that defend against infections and other invaders. When T cells detect a threat, they "wake up" and start multiplying into an army to destroy it. How T cells are triggered to multiply has been largely a mystery.

St. Jude scientists have solved a central piece of the puzzle: T cells become fully awake thanks to the actions of a specific protein complex. Named mTORC1, this complex instructs T cells to start burning sugar and making lipids. These metabolic

activities prompt the T cells to start multiplying into the army that fights an infection.

"Our results answer a long-standing question about how one branch of the immune system is called into action at the first sign of an infectious disease," said Hongbo Chi, PhD, of St. Jude Immunology. "Our data show that T cell metabolism could be targeted for therapeutic benefit in the treatment of asthma and other diseases." The findings appear in the journal *Immunity*.

Learning more about COGNITIVE DEFICITS

New research led by St. Jude scientists indicates that the academic struggles of some brain tumor survivors may be due to damaged "insulation" covering nerve cells in the brain. The damage may be caused by either the disease or its treatment.

The speed at which some medulloblastoma survivors process information declines dramatically following diagnosis and treatment of the brain tumor. Researchers found that patients' working memory and broad attention were less affected.

Results reinforce the importance of working closely with families and teachers to ensure survivors have the support and resources necessary to succeed. St. Jude researchers are also testing approaches to slow or prevent cognitive declines.

The research, led by Amar Gajjar, MD, St. Jude Oncology co-chair, and Shawna Palmer, PhD, formerly of Psychology, was published in the *Journal of Clinical Oncology*.

Making Life Better

By Kerry Healy

The Billie and George H. Ross Foundation's goal is simple: To improve life for St. Jude patients and families.



In his St. Jude hospital room, 10-year-old Joe Wilson uses one of the interactive systems provided by George and Billie Ross (inset). Kids can use the inpatient system for education and communication as well as entertainment.

Through the Billie and George H. Ross Foundation, one well-known couple seeks to make an immediate impact on the lives of children battling cancer and other life-threatening diseases at St. Jude Children's Research Hospital. Their motivation, they say, comes from their love of helping sick children.

"We want to do whatever we can to help the situation of these families and to make life easier for them," Billie says.

George, an accomplished attorney and author, is well known for his co-starring

says. "We were very impressed, and we are in a position to help, so we decided to do it."

The Billie and George H. Ross Foundation has helped fund a patient treatment room at St. Jude and has provided funding for a patient education and entertainment system for every inpatient room in the hospital.

"It's a wonderful communications device, both educational and fun, for children who have to stay in the hospital," George says. Recently, the foundation

role on Donald Trump's reality show, *The Apprentice*. The Rosses were first introduced to St. Jude at a fundraising event held at Trump's Mara-a-lago Club in Palm Beach, Florida. As any good lawyer would do, George thoroughly researched the hospital and liked what he saw.

"We looked at how St. Jude operates and the research they are involved in," he

also made a pledge to St. Jude for funding cardiopulmonary equipment.

George says the foundation's goals are simple: "It's about doing whatever we can do now to make life better for these children and their families," he says. "Those are the things that are on our short list."

In August of 2012, Billie and George visited the hospital, along with their daughter, Stephanie, and son-in-law, Tom. The family was overwhelmed by the experience.

"The care that was given to all the patients, the fact that no one pays—it was such an uplifting experience for all of us," Billie says.

The family found the philosophy of the St. Jude leadership and staff to be particularly remarkable.

"They don't look at something and say, 'We can't do this,' or 'We can't afford it,'" George says. "If there is a need for a child, they say, 'Let's do it, and we will figure out a way to pay for it.' To us, that philosophy is awe inspiring."

For George and Billie, there is no time like the present to help children and families battling cancer at St. Jude.

"A person would have to be hard hearted to not be touched by this," Billie says. George adds, "We do what we do because we are trying to help solve the problem of childhood cancer." ■

A Mother's STRENGTH

By Leigh Ann Roman

St. Jude celebrates the courage and tenacity of moms.

SETH DIXON



Seven-year-old Devin Young shares a quiet moment with his mom, Danielle.

Unless she has to work, Danielle Young usually spends Mother's Day with her sons and her mother, "doing whatever my mom wants to do."

But Danielle is likely to spend this Mother's Day at St. Jude Children's Research Hospital, where her 7-year-old son, Devin, is receiving treatment for a fast-growing tumor near the center of his brain.

As a single mother of two, Danielle is used to waking up ready to handle whatever comes her way.

"You just get up every morning and do what has to be done because there is not an extra person to lean on," she says.

Danielle's daily duties have changed drastically since last August, when doctors discovered Devin's illness was not a sinus problem, but a brain tumor.

"They were like, 'Get in this ambulance, you've got to go now,'" she remembers. "'Say your good-byes to

any family.'"

Danielle and Devin sped to Memphis, leaving her 9-year-old son, Donovan, at home with his grandmother.

After the biopsy confirmed cancer, surgeons removed as much of the tumor as possible. Then Devin began six weeks of radiation therapy at St. Jude. His chemotherapy treatment should be complete sometime this spring.

Danielle and Devin have been home just once since August, and the family's separation is difficult for her and her boys, who are best friends.

"For seven years, these two have had each other. They have never been separated and never even spent the night away from each other," she says.

Danielle talks to Donovan by telephone daily, and her care for Devin, who was also diagnosed with mild autism, is evident in her gentle tone. She is clearly Devin's rock.

With her easy laugh and down-to-

earth manner, Danielle carries calm into all situations. That

characteristic has benefited her during Devin's illness and her eight years in the U.S. Navy.

"I learned early [in the Navy] that crises happen, and there is no need to get upset. If you get upset and flustered during a crisis, you will probably make a mistake. That has helped me to keep calm during this," she says.

Throughout Devin's illness, Danielle has been thankful for the support of her mother, who is willing to move to Memphis if treatment continues past spring. And Danielle is appreciative of St. Jude.

"I'm extremely grateful to be able to get Devin such good treatment. The people here have been great," she says.

"I fully have faith that Devin will make it through this and be fine. But at this point, it's one day at a time," Danielle adds. "If things can change, they will."

St. Jude recognizes the strength of mothers everywhere. If you know an amazing mom like Danielle, you can honor her and support St. Jude by purchasing a Mother's Day Tribute card at stjude.org/mother. ■

*Honor an amazing mom
visit stjude.org/mother*



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—Carol Di Lorenzo

Their gift gives back.

*St. Jude patient Jorge
bone cancer,
at age 9*



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Fat Tuesday Fun

Child Life specialists Brittany O'Shea (at left) and Amanda Brody help 10-year-old Joshua Quist get into the Mardi Gras spirit at St. Jude. Joshua joined other patients and families in decorating masks and parading throughout the hospital. Employees lined hallways and clinical waiting areas along the parade route to throw and catch purple, green and gold beads. The parade ended in front of the hospital's cafeteria, Kay Kafe, but the party continued with refreshments for families and staff.



Finding cures. Saving children.